rheumatoids.

DR. CHENG: Let me try to gain a better understanding of your comments. If we have someone with rheumatoid arthritis and satisfactory soft tissue constraints, do you think this will work as well as--I know we're not supposed to compare with other devices--but I am asking you would it work as well as the other silastic component?

DR. NAIDU: My gut feeling is that it will, provided all the training and everything is done properly. That's my gut feeling if the soft tissue envelope is adequate. But I can't tell you that based on the data that has been provided. I know it is difficult to obtain such data. I know that we are working with a limited amount. And this is a significant advancement, too.

So I am left wrestling with this as to where I should go next, and the only thing I feel comfortable with at this point is the osteoarthritic and post-traumatic.

DR. SKINNER: Dr. Aboulafia?

DR. ABOULAFIA: I think we all recognize and share your opinion, and at least when I look at things before the FDA, everything is a risk-benefit and sort of a weighing of safety and efficacy, and

for things that represent significant potential harm, the threshold for approving efficacy might be very, very, very high; for something that appears by all parameters to be safe, the threshold might be different.

So as I wrestle with is this the perfect study, are there legitimate criticisms, did they prove beyond a reasonable statistical significance that it is going to function better or substantial equivalent, I try to think of what the risks are, and are you comfortable at least with the safety issues.

DR. NAIDU: I understand what you're saying, but unfortunately, even that's not--these are late-stage rheumatoid deformities that were presented in clinical series, and we're talking about reconstruction that I have to try to imagine at this point as to what the soft tissue envelope is.

Looking at the complications, at least for the osteoarthritic and post-traumatic group, I feel comfortable. For the rheumatoid arthritis and the SLE group, the data that is provided, 16 of the 22 needed reoperation within one year for soft tissue concerns. And you know, no matter how much

labeling you put in, these are challenging issues that you have to wrestle with.

I don't know what to say.

DR. SKINNER: Dr. Peimer, do you have some comments? If you don't, I do. I look at the early--I'll give you a minute--I look at the early to mid rheumatoid arthritis with destruction of the joint surface, with an intact soft tissue envelope, as being roughly equivalent to an osteoarthritic. And this is a patient who is typically too early for a Swanson, and they just basically have to suffer until they get worse.

So I look at it as an opportunity to help a patient earlier than you would otherwise. Synovectomy isn't going to help if the cartilage is destroyed. It looks to me like it walks like a duck, talks like a duck--it's an osteoarthritic.

Dr. Peimer?

DR. PEIMER: Why is it that osteoarthritics talk like ducks in California?

Actually, I'd like to ask Dr. Beckenbaugh a question, that is, in going back in these 16 people and doing the soft tissue reconstruction, drop the other shoe--then what happened? You had to go back, you had to rebalance, you had to do

some ligaments, you had to realign tendons.

DR. BECKENBAUGH: Yes, we did, I believe, mention that we did have to replace approximately half of them with silicone because the soft tissues were not reconstructible; and the long-term survival of the others was satisfactory.

When we looked at the options again of the risk versus the reward versus the efficacy and safety, we've got a lot of those covered. It seems to me like it's a very safe material. We have had virtually no major problems with it. If they fail, we can reconstruct them. And they are durable, and they act more like regular joints. It's just the kind of thing that in an early rheumatoid would offer us something to do for them, because we just can't do it right now. I'm not going to put a silicone in the types of patients I described to you. But if we've got a good soft tissue envelope that you've discussed, and that can be in a more advanced arthritic case, we can do this operation.

DR. SKINNER: Dr. Finnegan?

DR. FINNEGAN: Do you think that you just described a pilot project which allowed you to define the limitations of the material and that the next step, then, should e a prospective,

randomized, controlled--

DR. BECKENBAUGH: We really can't randomize and control this type of device, because there are different indications. I would not do a silicone device in the types of patients that I would do this operation in, so I don't think that's practical.

DR. FINNEGAN: But you could do standard of treatment.

DR. BECKENBAUGH: We have had a lot of experience which suggests that this is efficacious material in people with minimal soft tissue disease, and I wouldn't feel good about trying to randomize a person into silicone or this joint replacement.

DR. FINNEGAN: But you could randomize them into standard treatment, which is to follow them and this particular implant and then see how they do.

DR. BECKENBAUGH: I guess I don't understand that.

DR. FINNEGAN: Your standard of care right now for an early rheumatoid is to follow them, do hand therapy and medications, and not do any surgical intervention?

DR. BECKENBAUGH: Well, we--that's correct. We don't intervene until they get to a more severe state.

DR. FINNEGAN: Right. So you could do a 2-year follow-up, or you could do a prospective randomized study doing your standard of care for patients at the present time versus this implant and document differences.

DR. BECKENBAUGH: Well, you could, but what might you take the risk of doing? You might take the risk of treating that patient early with a device which we think is superior and switching them to a silicone device which we know is a salvage device--because if they progress, 2 years later, I can't do that operation on that patient.

DR. FINNEGAN: But the opposite side, which is what the panel has to look at, is that a number of implants have come through here, including for the hand population, which have resulted in catastrophic things that are difficult to fix down the road. So--

DR. BECKENBAUGH: Well, Dr. Naidu has discussed the catastrophic events and has gone through them in detail, but these are not excessive. What he has failed to emphasize from my

perspective is the dramatically good results that we have seen in extremely long-term follow-up. There is the difference in the way we look at this.

There is a prosthesis that we have had available to us that will let us do more than we can possibly do with silicone devices, and that's why we're here.

DR. SKINNER: Dr. Cheng?

DR. CHENG: I was just going to mention my opinion. I sympathize with Dr. Finnegan's and Dr. Naidu's comments. The data here, as I said before, has severe limitations, and it is very difficult to make a judgment on that.

So in my mind, it comes down to do you approve this product, or is there reason to--in other situations where I have dealt with this as a panel, we either go back to the sponsor and say "Go and do a prospective study"--this is what Dr. Finnegan is driving at--a prospective randomized study, the standard of care versus your product, and come back in 2 years and tell us which is better--or if it is equal or worse--hopefully, not.

So in my mind, does it warrant that at the present time, or does it warrant approval, and should we approve it in comparison to some other

times when we've just talked about approving something maybe too early and not having sufficient data.

My thought on this issue right now is that in comparison to those other times where there are perhaps six other devices that can do the same thing, and someone is trying to get another device on the market, this is a situation where there is no other device on the market--this is what I am hearing; that for rheumatoid arthritis, where there is cartilage destruction but not to the point where you want to do a constrained arthroplasty, or for the traumatic case, there is no alternative other than the standard of care, which is to, if it is rheumatoid, treat the patient medically or with therapy, or those other options I mentioned before, amputation and arthrodesis.

So it seems to me like there is some reason to think that there is an unmet need, if we put it that way, in the clinical population, and that's what I am hearing from this discussion, so that is the only reason for me to think maybe we ought to approve this with the given data, as inadequate as it is, as opposed to asking the sponsor to do a more rigorous study.

That's the way I'm trying to resolve this in my mind, because I have the same feeling that you do.

DR. SKINNER: Dr. Larntz?

DR. LARNTZ: One very small point. If they do a 2-year study, it's only a 2-year study. That's all. They won't have 10-year data.

DR. SKINNER: So you are implying that they aren't going to learn a whole lot more--

DR. LARNTZ: Well, we'll learn about the early parts of this intervention. We will not learn about the long-term effects of this intervention.

DR. SKINNER: Any more on indications and contraindications?

Dr. Witten, did we cover the indications adequately?

DR. WITTEN: Yes. Thank you.

DR. SKINNER: Are we ready for the open public session?

DR. WITTEN: Excuse me. We do have one other question about patient labeling, which is what additional information do they need to provide in their patient labeling, which are the information sheets to the patients.

DR. ABOULAFIA: Is there a document that we have been given that shows what the patient labeling is? Is there an easy way to find it on the CD?

DR. PEIMER: It's in Amendment 3, I think.

MR. DACEY: Page 116.

DR. PEIMER: That's correct; Amendment 3, page 116, Appendix 5. It is Amendment 3, Appendix 5, page 116.

DR. WITTEN: I think if the panel could just generally comment on what information they think would be important to provide in a patient information sheet, that would be helpful.

DR. CHENG: Haven't we already said what information that is? Haven't we answered that question?

DR. WITTEN: Well, you have been talking about the information that should go to the physician, I thought.

DR. CHENG: Is see, okay.

DR. WITTEN: Things like adequate soft tissue available isn't really patient information. But what do you think would be important to provide to patients as information about this device?

DR. ABOULAFIA: The only ones that I think

about--and I am not a big fan of necessarily patient information sheets--but something about the physical therapy and your postoperative course, and when do you call your doctor--if your finger becomes red, hot, swollen, painful, and you develop a fever, you should call your doctor. Other than that--even though you had no infections--I think those are appropriate.

DR. SKINNER: I think that's appropriate, too; an emphasis that the physical therapy program is very important in the process--or occupational therapy, whichever.

Are there any other comments about the patient labeling, page 117 and on?

Yes, Mr. Dacey. This is appropriate.

MR. DACEY: Yes, this kind of falls in my area of expertise. Clearly, the applicant has referred to the general patient labeling recommendations, and I always tend to sometimes agree and sometimes disagree with physician perspectives on these kinds of issues, because I have spent so many years dealing with patients and interfacing between physicians and patients. And of course, you have all heard "My doctor never tells me anything."

There are also some legal informed consent criteria that have to be met with these kinds of documents. But my experience has been that we always make assumptions that patients understand the words that we put on paper, and if you look at the Dokes [phonetic] study that I think goes back to 1993, about fifth grade reading and understanding abilities of the general population, the recommendations say eighth trade. I would still go back to the fifth grade. Plus, we have this huge, diverse population in which, in our section of the country alone, everything has to be translated into Spanish now on several different levels, and we are having extreme difficulty with that very issue and also with the Hmong populations.

But I was looking, and in the recommendations, it says "We believe it would be helpful to give the patient an easy-to-understand description of the procedure," and they followed the outline that was given. "The implant surgery will likely take a few hours. The surgeon will fit your finger with the correct size of the device and then implant it into the natural cavities of your finger bones." That is a description of the

procedure.

From a patient perspective, I favor uncomplicated words and uncomplicated pictures. This is an ideal spot to have a very uncomplicated little illustration. And I found some paragraphs where seven points were made in one paragraph, using very compound, complex sentence structures. I am a comma hunter--that goes back to my journalism days--if there is more than one comma in a sentence, you break up the sentence. And I found some that really lend themselves very well to bullet statements. But let's try to make it as easy as possible for patients, or consumers when they become patients, to have the very necessary option to call your doctor, talk to your doctor, ask questions. That's what all the TV commercials are saying right now in prime time--ask your doctor.

Let's give people the information that is going to help them in their decisionmaking and understanding. I can see in the hand therapy part of this an illustrated time line of what to expect across a period of time, because I was not aware of the 4 to 6-week recovery period. That's longer than bypass surgery for some people now.

So in summary, I would just say uncomplicated words, uncomplicated pictures, and keep in mind that patients really don't understand abstract ideas, and that whatever we document is still no substitute for that one-on-one contact and the skill training that patients are going to need.

DR. SKINNER: Just one comment about that, Mr. Dacey. This is an operation, a procedure that hasn't been done for some time, and it is obviously in a state of evolution if it is going to be done. And to put this in a patient brochure that is approved by the FDA that can't easily be changed could result in tying the physician's hands in terms of postoperative management. I would rather leave it as vague as possible from that viewpoint. But I would certainly go along with a picture or even an x-ray. A lot of the population is very sophisticated and watches television, sees these on TV.

MR. DACEY: In the community where I live, where I have consultations, I've got astrophysicists as patients, and the line of questions I get is a lot different than down the road, with a totally different population. While I agree that any time you put the words and pictures

on paper, you tend to freeze the design until such time as it gets revised, I would not suggest that you handicap the surgeon in any way, but I feel there is a middle ground that this can be accomplished. The lifetime of any document is not 6 months.

DR. SKINNER: Any other comments on patient labeling?

DR. ABOULAFIA: It's not incredibly germane--people use the term "conservative" to mean "nonoperative," and I don't think that that necessarily follows, so I don't like "conservative therapy" to mean nonoperative.

DR. SKINNER: Dr. Witten, have we addressed your issues?

DR. WITTEN: Yes. Thank you.

DR. ABOULAFIA: Mr. Chairman, would it be appropriate to make a motion regarding the PMA before us at this point?

DR. SKINNER: Not quite.

DR. ABOULAFIA: Okay.

DR. SKINNER: We will now proceed with the open public session of this meeting. I would like to ask at this time that all persons addressing the panel come forward and speak clearly into the

microphone as the transcriptionist is dependent on this means of providing an accurate record of this meeting. We are requesting that all persons making statements during the open public session of the meeting disclose which company they represent and whether they have financial interests in any medical device company.

Before making your presentation to the panel, in addition to stating your name and affiliation, please state the nature of your financial interest, if any.

Is there anyone wishing to address the panel?

[No response.]

DR. SKINNER: Seeing no hands rise, we will have a 5-minute break and then proceed with potential comments from the sponsor.

[Short break.]

DR. SKINNER: Let's get started and wrap this up.

We have discussed the open public session, and no one from the public wanted to speak.

At this time, I would like to ask Ascension if they have any final comments before the panel proceeds with voting on the MCP finger

joint premarket approval application.

DR. KLAWITTER: Thank you.

I would like to take the opportunity to thank everyone for their careful consideration.

DR. SKINNER: I would now like to ask Mr. Haney Demian to read the voting instructions for the panel.

MR. DEMIAN: I will now provide you with the panel recommendations options for the premarket approval application.

The Medical Device Amendments to the Federal Food, Drug and Cosmetic Act require that the Food and Drug Administration obtain a recommendation from outside expert advisory panel on designated medical device premarket approval applications that are filed with the agency. The PMA must stand on its own merits, and the recommendations supported by safety and effectiveness data in the application or by applicable publicly available information.

Safety is defined in the Act as "reasonable assurance, based on valid scientific evidence, that the probable benefits to health under the conditions of use outweighs any probable risks."

Effectiveness is defined as "reasonable assurance that in a significant portion of the population, the use of the device for its intended uses and conditions of use when labeled will provide clinically significant results."

Your recommendation options for the vote are as follows:

1) Approval. There are no conditions attached.

2) Approvable with conditions. You may recommend that the PMA be found approvable subject to specified conditions such as resolution of clearly identified deficiencies which have been cited by you or FDA staff.

Prior to voting, all conditions are discussed by the panel and listed by the panel chair. You may specify what type of follow-up information is needed as a condition of approval in your recommendation. The panel may request specific follow-up be done through a homework assignment to the primary lead reviewers of the application or to other specified panel members. However, a formal discussion of the application at a future panel meeting is usually not held.

If you recommend post-approval

requirements be imposed as a condition of approval, then your recommendation should address the following points: the purpose of the requirement, the number of subjects to evaluated, and the types of reports that should be required to be submitted.

Your third option is Not Approvable. Of the five reasons that the Act specifies for denial of approval, the following three reasons are applicable to panel deliberations: a) the data do not provide reasonable assurance that the device is safe under the conditions of use prescribed, recommended, or suggested in the proposed labeling; b) reasonable assurance has not been given that the device is effective under the conditions of prescribed, recommended, or suggested in the labeling; and c) based on a fair evaluation of all material facts in your discussions, you believe the proposed labeling to be false and misleading.

If you recommend that the application is not approvable for any of these reasons stated, then we ask you to identify the measures you think are necessary for the application to be placed in approvable form.

It is noted that following the vote, the chair will ask each panel member to present a brief

statement outlining their reasons for their vote. Traditionally, the Consumer and Industry Representatives do not vote, and Dr. Skinner as chairman only votes in the case of a tie.

Dr. Skinner?

DR. SKINNER: Thank you, Mr. Demian.

Before beginning the voting process, I would like to mention for both the panel's benefit and for the record that the votes taken are votes in favor of or against the motion made by the panel. Votes are not for or against the product.

Is there a motion?

MR. DEMIAN: We are going to allow Dr. Naidu to provide that motion since he was the lead panel clinical reviewer.

DR. SKINNER: Dr. Naidu.

DR. NAIDU: Yes. The motion is to approve with conditions.

The conditions that I list are as follows, and my reasoning is based on all the reasons that I have given for the last several hours.

DR. SKINNER: Let's just stick with the strict motion for right now, and we'll go into a discussion phase after we have a second.

DR. NAIDU: Okay. The conditions that I

impose for this device that I would like to see--we have a vacuum in the hand world; we have no other alternative. This is a bold step. We need something different for post-traumatic and osteoarthritic patients.

The device was initially intended for high-demand patients, great range of motion. I think this device has great promise in that direction.

Therefore, the condition that I would impose is that this be approved for osteoarthritic and post-traumatic arthritic patients.

Thanks.

DR. SKINNER: Is there a second to that motion?

[No response.]

DR. SKINNER: Hearing no second, is there another motion?

Dr. Aboulafia?

DR. ABOULAFIA: I'd like to introduce a motion to approve the PMA presented before us, Number P000057, with approval with conditions.

The conditions I would request are those which have already been stipulated under the section of contraindications and indications, the

contraindications being severe deformity and rheumatoid arthritis, unreconstructable radial-collateral ligament, extension lag greater than 45 degrees, ulnar deviation greater than 30 degrees or one centimeter of subluxation, as well as specific onsite training as recommended by the sponsor during the discussion portion of this PMA presentation.

And one cautionary portion about small and ring digit, period.

DR. WRIGHT: Would you repeat the last three?

DR. ABOULAFIA: With a cautionary statement about results in the small and ring digit.

DR. SKINNER: Is there a second for that motion?

DR. LI: Could I have a clarification--is that going to be the limit of the approvable with conditions?

DR. SKINNER: No. After there is a second, you can make an amendment, but until there is a second--

DR. LI: Then, I second it.

DR. SKINNER: Okay. There is a second for

the motion. Now we can go on to discussion.

DR. PEIMER: I'd like to propose an amendment. I think amendments take precedence.

DR. SKINNER: I don't know if that's the case.

MR. DEMIAN: No. I think we have the discussion, and then Dr. Aboulafia would be able to amend his original motion as he saw appropriate.

DR. SKINNER: Dr. Larntz is always very brief.

DR. LARNTZ: We need post-approval study for this device. We have not enough data for this device, so we have to have a post-approval study. I will put out some numbers--they are subject to modification--but I would say we need a 100-patient follow-up in the OA group for 5 years. I would say we need a 100-patient follow-up in the RA group for 5 years. I would say that it includes at least five centers, not including Mayo Clinic, Rochester, and I would say that it obviously needs to be a prospective study and needs to collect detailed adverse event information with follow-up at one, 3, and 5 years for patients.

DR. SKINNER: Dr. Witten?

DR. WITTEN: You need to state the purpose

of the study.

DR. LARNTZ: The purpose of the study is to fully understand the adverse event profile for this device.

DR. WITTEN: I just want to make a clarification about post-approval studies. When you are voting, you are voting on whether there is reasonable assurance of safety and effectiveness or--Haney could read the language. So if you want some post-approval information--if you vote that there is reasonable assurance of safety and effectiveness, then you need to focus what your post-approval question is.

MR. DEMIAN: The points that should be considered in a post-approval study are as follows: the purpose of the requirement, the number of subjects to be evaluated, and the types of reports that should be required to be submitted. So I think you've done two of them; now you need to do the last one. Tell us what type of reports should be required, and what would be in those reports.

DR. LARNTZ: I thought I said that. I thought we were going to get adverse event information.

DR. SKINNER: Would that not be

accomplished with the MDR process?

DR. LARNTZ: Not at all; not prospective followed in the same way, no.

DR. SKINNER: Could I ask one more question? Why would you want to do more than what would typically be required for a PMA?

DR. LARNTZ: I just picked numbers, and I said that's negotiable.

DR. SKINNER: Five years is way more than you would typically need for a PMA. You'd need 2 years for a PMA.

DR. LARNTZ: Oh--this is a PMA, and we have some--

DR. SKINNER: But you are talking about approving it and then requiring a PMA.

DR. LARNTZ: No. I'm getting follow-up information on these patients. That's all.

DR. SKINNER: Comments?

Dr. Peimer?

DR. PEIMER: From my view of the data presented and with specific reference to what Dr. Naidu discerned and what Dr. Beckenbaugh and Ascension discussed as the peri-implant implications, especially in the early phase, I think the issues relative to sorting out the better

candidates--I hate to say "best"--in the rheumatoid population, which we really want to find out to refine the indications for this, could be served in a 2-year study, and I would leave it to you, Kinley, to tell us what the "N" should be, but I would look at a 2-year study, and I like the idea of multiple sites in addition to the Mayo Clinic. Since the majority of the reoperations occurred in that first 12 months, we may actually not even need that second year to uncover what we are trying to find out.

But that is the amendment I would have made.

DR. LARNTZ: Two years is fine with me. I would accept that, no problem. And the "N"--I am worried about the OA group because of the very small number of patients that we have data on. It has been pointed out repeatedly. And a smaller "N"--depending on what we think the event rates are going to be for these things that we are worried about, 50 patients in each group would be fine with me. That would be fine.

DR. SKINNER: Dr. Aboulafia?

DR. ABOULAFIA: My guess is that you are going to have trouble accruing 50 patients in a

reasonable period of time. Sponsor can tell me if I am mistaken there. Dr. Beckenbaugh has done 4, along with Dr. Linscheid, at a reasonably busy academic institution. That's over a period of how many years--12, 14.

Dr. BECKENBAUGH: That's correct.

DR. ABOULAFIA: So to expect you to get 50 OAs, depending on how many people you plan on training, do you think Dr. Larntz is going to come back with those kinds of numbers? In other words, it isn't going to happen. We can ask them to do it, and I think they are honest enough--

DR. SKINNER: Dr. Beckenbaugh, can you answer the question?

DR. BECKENBAUGH: I think it's very difficult in a post-study perspective to enroll patients. The patients will generally have to have information that may discourage them from undergoing surgery. Perhaps there is paperwork, there are commitments. I can guarantee you we will be studying these patients extremely closely as we are in our other endeavors, but I would like to think we have the academic honesty to do this on our own.

DR. SKINNER: Dr. Finnegan?

DR. FINNEGAN: Actually, I think Doug was before me.

DR. WRIGHT: Thank you.

Dr. Witten, didn't we talk about labeling before, and I thought everyone as in agreement that we were going to add to the label the indications and contraindications; correct? That's going to be approved; that was from Question 2.

DR. WITTEN: Well, you can certainly use the information you generated in Question 2, but when you have your vote--that was a discussion; I don't know that there was a vote on it. It will have to be specifically included if that's the information you want.

DR. WRIGHT: I guess my question is could we not just vote--I thought that labeling was going to be part of what we had talked about. My inclination would be to put forth to vote as submitted and then make that part of the labeling restriction and not have it have anything to do with the voting.

DR. SKINNER: Dr. Aboulafia?

DR. ABOULAFIA: My understanding is that that is not the case; that if there are things that you believe must be in the labeling which are not

in the sponsor's proposal, and that would influence your decision to improve the PMA or not approve the PMA, then it has to be specified.

DR. WRIGHT: Right. That's already in their proposal, though, now.

DR. ABOULAFIA: It is not.

DR. WRIGHT: I thought they have a label in that talks about what the indications and relative contraindications are.

DR. ABOULAFIA: No. In the ones that I mentioned--and I just took it off the CDROM because I pulled it out--the things that came up in discussion and sponsor can address are not addressed in their application.

DR. WRIGHT: Do they have any restrictions on their labeling?

DR. ABOULAFIA: Yes. They say contraindications are severe bone loss, joint sepsis, neurologic, skin, or bone condition, and there is one more--I just took it off the--severe rheumatoid is not listed as a contraindication, but it has come up in discussion that sponsor--actually, it was their idea, and I am just talking about what they said.

I think they were very academically honest

and discussed what the limitations of the product were, and that's why I quoted their words when I used what I would include as contraindications.

DR. SKINNER: I think I'd feel more comfortable with those in the motion also.

DR. WRIGHT: You'd feel more comfortable.

DR. SKINNER: Even though I won't vote on it unless there is a tie.

DR. WRIGHT: Okay. I just thought that I saw a table already listing indications and contraindications.

DR. ABOULAFIA: It's 6.3. If you guys want to tell me, I'll load it up real fast.

MR. STRZEPA: This is Peter Strzepa.

I'll just read the contraindications. "Inadequate bone stock, indications of active sepsis or infection in the MCP joint, nonfunction or irreparable MCP musculotendinous system, interference with or by other prostheses, procedures requiring modification of the prosthesis, and skin, bone, circulatory, or other neurological deficiency."

DR. SKINNER: Dr. Finnegan?

DR. FINNEGAN: Thank you.

Actually, the clarification for the FDA is

what I would like to ask. I think, Dr. Witten, what you see here is a group who sees an implant that appeals to them; there is a clinical indication for which there are not a lot of other options, but there are some difficulties in making a decision based on the material that we have.

What are the other options that would be available to the company if we elected to not do this?

DR. WITTEN: Well, I'll answer that, but with a caveat.

DR. FINNEGAN: You always answer with a caveat, so that's okay.

DR. WITTEN: Well, I'm with the FDA.

I just want to mention that we are asking you to make your decision based on the data available to you, so we want you to make your decision on reasonable assurance of safety and effectiveness based on what is in the application. That is what we are asking.

So you are asking me in general for a product that is--

DR. FINNEGAN: We don't want to see this die; that is our concern. But I would say, just listening to people around the table, that that is

a significant concern.

DR. WITTEN: Okay. Well, generically, the routes of availability for Class III products that are not Class III pre-amendments--including this one, I'd say, with some exceptions which are irrelevant here--the route to market for Class III products in general is PMA, which is this. There are other kinds of applications which include something called a "product development protocol" by which a sponsor can agree with the FDA prospectively on what their development plan for that product would be and then, at the end of that time, if they fulfill the conditions of the PDP, they can go to market. That is to say, they don't have to come back for an approval; if they have all their testing specified and they meet their endpoints, they go to market. So that is a second possibility.

Of course, there is Investigational Device Exemption by which devices can be available and also, if the population is small enough, Humanitarian Device Exemption applications also, which is for populations of 4,000 patients or less a year in this country would be eligible.

DR. FINNEGAN: And how onerous is the

PDP--the IDE, I understand you have a time limit of a maximum of 30 days before you answer them. What about the PDP?

DR. WITTEN: Well, it's hard for me to answer the question of "onerous." The sponsor makes an application, we discuss it with them; in general, we would bring it to a panel before approval for discussion, depending on what our questions were. It is a process; it is hard for me to answer.

DR. SKINNER: A PDP is simply a PMA that is done prospectively.

DR. WITTEN: Right; exactly.

DR. SKINNER: That's the only difference is that basically, you are getting a promise from the FDA up front that this is what is required so that when Haney quits and Celia quits and all those people quite and you've got another set of FDA people, you don't have to wrestle with new conclusions.

DR. FINNEGAN: Is that an option for us?

DR. WITTEN: You don't have the option to vote on a PDP because that's not the application you have in front of you. That's obviously something that you could suggest. But we are

asking you to vote on this application that you have in front of you.

I was just answering the question that you asked about what were the regulatory options for this kind of application--or, sorry--for which this device would be eligible.

DR. SKINNER: Dr. Peimer?

DR. PEIMER: We seem to have gone south a little bit on the numbers and what was reasonable to do. I don't think we'd have a difficult time at multicenters collecting data on rheumatoids collecting data on rheumatoids, and if an "N" of--you've got to help me with this, Kinley--let me finish, and I think I'll make it easy for you--

DR. LARNTZ: Yes. Go ahead.

DR. PEIMER: What I'm going to suggest is that we pick an "N" for the rheumatoid data and as many osteoarthritics as are collected in that time--that's the "N" for the osteoarthritics.

I have no doubt that Bob Beckenbaugh's experience and that of his colleagues at the Mayo Clinic will be adequately reported. I think it will be more quickly reported if multiple sites are enlisted in the process.

DR. LARNTZ: I have no problem with that.

And if I say 50 RAs and however many OAs collected during the time period until the 50th is enrolled--that's what you're talking about--I have no problem with that.

DR. SKINNER: Let me interrupt for a second. Haney has brought to my attention again that if we are going to have a postmarketing study, we have got to define what information we are going to get out of that study, and that information cannot be safety and efficacy, because we are voting on that right now.

So what information do we want, and if we can't get any information except safety and efficacy, we should not have a study. What information do we want?

DR. ABOULAFIA: I'll try to make it easy. I'm not sure that I am all in favor of post-approval study, but I think it might bring people together without being onerous on industry.

Why don't we say that we'll collect prospective data on the next 100 patients, with the endpoints being range of motion, revision, infection, and fracture, bone fracture or implant fracture. And the purpose of that is--I know I'm stretching; let me think--the purpose of that is to

see if other surgeons can reproduce the same excellent results that have been achieved at a given center.

DR. SKINNER: Let me make another suggestion. Suppose we take 50 patients followed for a year, and in those 50 patients, we define the indications. That's not a safety issue is it, or efficacy?

MR. DEMIAN: Can you redirect that question to Dr. Witten?

DR. SKINNER: Dr. Witten, we take 50 patients for one year, and in those 50 patients, we define the indications for the procedure more clearly.

DR. WITTEN: Well, you need to decide whether or not you think that the information in the application, with the indication either as written or as amended by you--indication can be written--with a reasonable assurance of safety and effectiveness. And if you think you can, that leads you to one conclusion; if you think you need a study to define indications, that is part of what you are voting on when you vote that something is safe and effective. It is safe and effective for specific indications. So that really depends

on--you can recommend a study, but what that means to us about what we know about the product is different.

DR. SKINNER: I have been here for 4 years, and we have asked for studies in the past, and I don't remember this being a problem before. Were we doing wrong?

DR. WITTEN: I don't--I am not saying anything inconsistent with what we say in general, but I don't want to go on and talk about what we have done with other products. I think our message has really been consistent about post-approval studies being to answer a focused question on a product whose safety and effectiveness for a specific indication are felt by the panel already to be understood or demonstrated by the data in the application.

DR. SKINNER: Dr. Aboulafia?

DR. ABOULAFIA: Let me just say for the record that my intention to look at a post-approval study was in the interest of compromise and that my original motion sticks and that I believe with the original motion as proposed for the indications given and the contraindications given, it is safe and effective.

DR. SKINNER: Discussion on that?

Dr. Larntz?

DR. LARNTZ: No more comments.

DR. SKINNER: Dr. Cheng?

DR. CHENG: I have a question for Dr. Witten. I don't understand the background of this application. This device was implanted from 1979 to 1987. It is now 2001, 14 years later. What happened between 1987 and 2001, and why are we looking at this in 2001? I'm sure there are some issues that are going on here that I am just not aware of, and I am wondering if I may be privy to that--was it on the market during that time? Was it taken off the market, and that's why the company was formed? What has happened here?

DR. WITTEN: I can't--it hasn't been on the market; it hasn't been on the market, and I--

DR. CHENG: Since when?

DR. WITTEN: It has never been commercially available.

DR. CHENG: So how was it put in, then, before--under an IDE?

DR. WITTEN: The initial implantations, I think--although sponsor probably knows the history better than I do--were prior to the IDE regulations

being in effect.

DR. CHENG: So it is a pre-amendment device.

DR. WITTEN: No. The Medical Device Amendments were in 1976, and I'm sorry I don't know the exact time we had the IDE regulations, but they--okay, '85. So someone else here knows better than I do.

And what happened between--I don't know that there are any specific issues. I am aware of the application and the scientific issues we have brought up today. I don't know of anything else specific that would be useful to know, and I'm not sure it would be relevant to the discussion anyway. I don't know if the sponsor has anything to add. I think that what is in front of you is what you need to consider, not anything else--and I'm not even sure what that something else would be.

DR. SKINNER: Any other discussion?

Dr. Li?

DR. LI: Can it be discussion on this postmarket surveillance, or any other discussion--

DR. SKINNER: To my understanding, we have discussed the possibility of a postmarketing study, and we can't seem to find a way to do that without

invoking safety and efficacy. So Dr. Aboulafia modified his proposal to not include the postmarketing study and wants to go from there. So if there is no more discussion, we'll vote on that.

DR. LI: I have an amendment, or I'd like to add a condition if that is appropriate.

DR. SKINNER: Okay.

DR. LI: And I don't think it is onerous on the industry at all--in fact, you may already have the answer. But I just have this kind of lingering "i" that I want to dot, that it has been 14 years since these devices were made that were put in, and it could be that actually, your current methods of manufacturing and production are even better than they were, but there is actually no direct comparison. In the two materials and design areas we have had the most discussion of, wear and fatigue and fracture, we only have the data from the current proposed device; we have no comparison back to the earlier device for which we have the clinical information.

So my question is in particularly those area of wear, fatigue and fracture, to make some connection between their current Ascension device and their original MCP device, however that might

be possible.

DR. SKINNER: You are implying that the present testing methods that they devised are not appropriate, or--

DR. LI: No. I am implying that the material isn't the same. I have no basis for comparison. In other words, we have one set of clinical data with the original MCP device, which was made with one set of materials and design, for which we have clinical data; and then, most of the preclinical data we have now is on the Ascension MCP device. So we have clinical data on one side, and we have materials and characterization on the other side, but it is not the same device.

So for instance, a specific example--they provided a fracture requirement range of somewhere between 1.0 and 2.6, but that is for their new device. I have no idea what those fracture ranges were for the old device. And we know the old ones didn't fracture--it's not that I have a fracture concern--but I would like to have a warm and fuzzy feeling that the current fracture values are similar to the ones they had before.

DR. SKINNER: Dr. Klawitter, do you have any inkling?

DR. KLAWITTER: This was a concern to us, and we did address this issue. We had some retrieved implants--not many of them--that were intact. We had developed the ability to model these using finite element techniques. We created finite element techniques of the current device that you are considering today, and we developed finite element models of the retrieved devices.

We strain-gauged multiple devices of retrieved and the currently existing device that you are considering. We were able to confirm through laboratory tests and load strain measurements that the models were predictive within approximately 5 percent, which I think is a very good concurrence with that type of prediction.

We also established failure criteria by doing load-to-failure tests with the current materials, which we feel are characteristic of what had been used in the past, because both of the strength criteria are very similar. Based on those measurements and using those fracture criteria, we established that the current device has equal or greater than fracture strength on the stem, using the same type of test.

So I personally am very confident, and I

think the information that we have given you shows beyond any reasonable doubt that in the current device that we have, the stem is at least as strong if not stronger than what was used in the patients in the late 1979 to mid-1980s period.

We did not have enough of these historic devices so that we could actually conduct fracture tests, but we have confirmed the results of the FDA analysis, and we have used those in subsequent ways, and I am very confident in those results, and they were included in the materials supplied.

DR. SKINNER: Any other comments before we move to a vote?

Dr. Cheng?

DR. CHENG: Yes. I think it is important to have some postmarket surveillance, and the reason I say that is because I think the way to get that done--otherwise, I could not approve the motion in my own mind--the reason I say that is because I think that it is weak, and we need to know whether there are complications or risks that are unknown. Like we said, the osteoarthritic patients--it's a tiny number of people. If this goes into another 20 to 25 people in the next 3 or 4 years around the country, people will want to

know if there are risks or complications that develop that we don't know about today. And I think that is the reason to do the postmarket surveillance and see that.

It does make it more onerous for the company, but I think it is necessary, and I think it mandates that the company follow this along and provide the funds to do so.

DR. SKINNER: Dr. Aboulafia?

DR. ABOULAFIA: I wonder if you would be satisfied with one of the lead clinical investigator's word that he intends to collect the data prospectively, in a scientifically and academically honest method and report his findings or their findings. It sounds like he is going to be training specific people who will be almost like his little fellows, going out around the country and doing this, and that it is not going to be something that is available to everyone; there will be a limited number of people doing it. And I think they will be looking at "N". Some of these issues are addressed with routine surveillance. When complications arise in products that are FDA-approved, they are appreciated by reporting standards that are in place.

DR. CHENG: Well, we all know that the threshold for MDR [phonetic] to catch something is much higher than that. And I have no qualms about the academic integrity of Dr. Beckenbaugh and following the patients along. But making this a requirement does provide the resources for doing that. Otherwise, where is the resource? It takes time, it takes money, it takes resources to do this. Where does it come from?

DR. WRIGHT: I think they have already given us a very long-term study. They have 10 years' follow-up on some of these people. So any postmarketing surveillance that we're going to give them is not going to be that far. This is unique in that I think they have bent over backward to demonstrate a lot of the problems that they have had. I think they have been pretty honest with us. So I don't think there are any snakes in the grass with this product. I don't think there is going to be something that is going to pop up 100 years from now. I think they have pretty long follow-up on this, and it seems to illustrate most of the things that can go wrong.

DR. SKINNER: Dr. Larntz?

DR. LARNTZ: I have no doubt the Mayo

Clinic will follow these patients and do a very good job. I have absolutely no doubt. I think it is important if we are going to do some postmarket study to do it in other centers to see how other physicians would handle the new device. That's all.

DR. SKINNER: I think we are spiraling to an end here. I want Dr. Aboulafia to reiterate his motion, and I think we should vote on it. I should call the question or ask for someone to call the question.

DR. ABOULAFIA: And I'm going to try to do it, but I'm not sure how you're going to go with this. I'm going to try to leave post-approval studies out, and I'm going to keep the amendment as I initially proposed it, and that is that I would make a motion to approve the PMA before us presented by Ascension, PMA Number 000057, for the Ascension MCP joint replacement device, with the conditions of better defining the indications, which include specific onsite training with one of us, a contraindication of severe deformity in rheumatoid arthritis, a contraindication of incompetent and inability to reconstruct the radial-collateral ligament, extensor lag of greater

doesn't carry for that, then somebody else would reintroduce a new motion.

DR. SKINNER: The difficulty with that postmarket surveillance thing was that we couldn't come up with a way of saying that we would get information out of it other than safety and efficacy, because that's what we're voting on right here.

DR. CHENG: Right, but looking for unknown risks that have yet to be problems--

DR. SKINNER: That's the problem, you see. You're talking about safety.

DR. CHENG: That's fine, but let's say people die of poisoning from this thing--I mean, that's far-fetched--

DR. ABOULAFIA: Let me answer that in the context of how Mr. Chairman presented it to you. They have already given us data that people are not going to die of poisoning, and I feel comfortable with the data presented that people are not going to die of poisoning that will not be addressed by any postmarketing surveillance study, because we have 10-year follow-up, and any postmarketing surveillance study is going to only go out to 2 years.

DR. SKINNER: Okay.

DR. CHENG: I think the reason for it is that, from what I hear from the discussion among the panel, that is rather marginal. I think many people on the panel feel that there is a place for this product, but they don't feel completely comfortable given what is in their hands at the moment in time.

DR. ABOULAFIA: I think that's why the conditions imposed are for a very specific group of patients.

DR. SKINNER: I think we have got to go to a vote here.

Dr. Larntz--wait a minute--the patient representative can vote--

MR. DEMIAN: No.

DR. SKINNER: No. Only panel members.

MR. DEMIAN: Only panel members.

DR. SKINNER: Okay. Dr. Larntz?

DR. LARNTZ: Yes.

DR. SKINNER: Dr. Cheng?

DR. CHENG: No.

DR. SKINNER: Dr. Wright?

DR. WRIGHT: Yes.

DR. SKINNER: Dr. Lyons?

DR. LYONS: Yes.

DR. SKINNER: Dr. Finnegan?

DR. FINNEGAN: Unfortunately, no.

DR. SKINNER: Dr. Naidu?

DR. NAIDU: The motion--I can't accept it--no.

DR. SKINNER: Dr. Li?

DR. LI: Yes.

DR. SKINNER: Dr. Peimer?

DR. PEIMER: Yes.

DR. SKINNER: Dr. Aboulafia?

DR. ABOULAFIA: Yes.

MR. DEMIAN: Six to three.

DR. SKINNER: It passes six to three.

MR. DEMIAN: It passes six to three.

Now you are going to go around the room and vote on each specific condition.

DR. SKINNER: Okay. Let's try to do this quickly.

First of all, a contraindication of severe deformity in rheumatoid arthritis. That is condition number one.

DR. ABOULAFIA: My vote is yes on every one.

DR. PEIMER: My vote is yes on every one.

DR. SKINNER: Dr. Li?

DR. LI: Yes on every one.

DR. NAIDU: Yes.

DR. FINNEGAN: Yes on every one.

DR. LYONS: Yes on every one.

DR. WRIGHT: Yes.

DR. CHENG: Yes to all the conditions.

DR. LARNTZ: Yes to all the conditions.

DR. SKINNER: Now we have the discussion of why the voted yes.

MR. DEMIAN: They can provide their comments--

DR. SKINNER: If they want to.

MR. DEMIAN: --yes--on the way you voted. Just go around the room, and if you want to provide anything else, you can; if not, that's fine.

DR. WITTEN: Excuse me--are they going to explain the way they voted for both questions?

MR. DEMIAN: Yes.

DR. WITTEN: For both--whether or not it is approvable with conditions and on the conditions?

MR. DEMIAN: Yes.

DR. SKINNER: Okay. Dr. Larntz, do you want to start?

DR. LARNTZ: I voted yes because I believe this device will be useful to patients; I am convinced of that from the clinical information provided here. I obviously believe that we need to gather more information about this device; I'm sure that will be done and presented in the peer-reviewed literature. And I think the conditions make it very clear that this panel thought very carefully about the subpopulations for whom this device would be intended, and I think the indications are specific for those subpopulations.

DR. SKINNER: Dr. Cheng?

DR. CHENG: I voted no because I thought the product should be approved with the study, as I said, afterward, that should be done to gather more information. I think there is a place for this product. It is analogous--if I make the comparison to the knee, I'm sure the hand surgeons would shudder--but it's like having a hinged knee or nothing, and here is a semi-constrained device that given the data that we have, I feel it's okay to use.

So that's the reason why the vote came out "no" because of Albert's amendment, or Albert's--

DR. SKINNER: And regarding the

conditions, you felt that if it was going to be "yes," the conditions were appropriate?

DR. CHENG: Yes, I thought they were appropriate, yes.

DR. SKINNER: Dr. Wright?

DR. WRIGHT: I voted yes because I think it's not a perfect implant, but I think it has some demonstrated utility. I think the data seems to support all the conditions that we put on it.

DR. SKINNER: Okay. Dr. Lyons?

DR. LYONS: I agree with that.

DR. SKINNER: Dr. Finnegan, closing comments?

DR. FINNEGAN: Just reiterating, there is not enough data for me to make a comfortable decision, but if it is approved, there is no question that it meets the conditions.

DR. SKINNER: Thank you.

Dr. Naidu?

DR. NAIDU: I voted no mainly because of all the reasons that I previously stated. The long-term complications are high in the rheumatoid population, and the other thing is that postmarket survey as requested by Dr. Cheng would have been useful in light of long-term complications.

I think this device is very useful for the high-demand post-traumatic and osteoarthritic patient. I think its indications are guarded in rheumatoid patients. The indications have changed from the data that was presented and from the presentation that was in front of the panel today.

There is a high complication rate, 40 percent success at 7 years' follow-up, and it is hard for me as a hand surgeon; although I would like to see something new in the hand arena, in light of the motion that was made, I had to say "no". But I think this device has great promise.

DR. SKINNER: Dr. Li?

DR. LI: I thought the device was well-thought-out. The preclinical testing was appropriate. My only--I'll go back to my main concern, that we have one set of test data and one set of clinical data not in the same material. I think it is unlikely there is a problem there, but anything you can do to bolster up that connection I think could only be positive.

DR. SKINNER: Dr. Peimer?

DR. PEIMER: Dr. Larntz said it best, and it need not be repeated. I agree with his description and conditions. I would just beg the

manufacture never to use the word "cosmesis" and never wear their vests inside their pants.

DR. SKINNER: Dr. Aboulafia?

DR. ABOULAFIA: I'd say that I agree with Dr. Cheng and Naidu but came to a different conclusion, and the remainder of my comments are on record already.

DR. SKINNER: Thank you.

The recommendation of the panel is that the premarket approval application for Ascension's MCP finger joint be recommended for approval with the conditions that have already been specified.

Executive Secretary?

MR. DEMIAN: I would like to thank all the panel members for their time and effort and energy in reviewing this material and their participation on the FDA panel. All of your efforts are truly appreciated.

At this time, I would remind all panel members that if you want the review material and any notes that you may have taken destroyed, please leave it in front of you.

On behalf of FDA, I would like to thank the entire panel.

This meeting is adjourned.

[Whereupon, at 3:55 p.m., the proceedings were concluded.]

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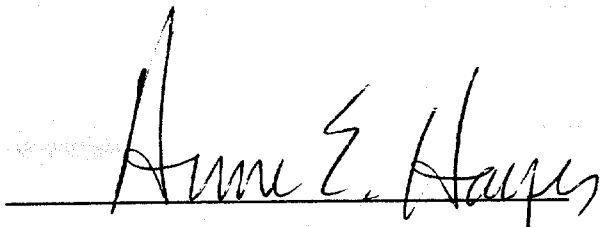
CERTIFICATE

I, **ANNE E. HAYES**, the Official Court Reporter for Miller Reporting Company, Inc., hereby certify that I recorded the foregoing proceedings; that the proceedings have been reduced to typewriting by me, or under my direction and that the foregoing transcript is a correct and accurate record of the proceedings to the best of my knowledge, ability and belief.



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